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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/973,375	10/09/2001	Donald Gerald Stein	07157/239838 (5543-17)	5877

826 7590 08/24/2006

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/973,375	STEIN ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12, 14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-12, 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/21/2006 has been entered.

The Amendment received on 04/21/2006, amended claims 1, and 16.

Currently, claims 1-12 and 14-20 are pending in this application.

Claims 1-12 and 14-20 as amended now are examined on the merits herein.

Upon further consideration, and in view of new ground(s) of rejection, the rejections made in the Final-Office Action dated 06/24/2005 are herein withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roof et al., (*Molecular and Chem. Neuropathology*, 1997, vol.31, 1-11, of record), in view of Backstrom et al. (US 6,455,516, PTO-892), and Gee et al. (Re. 35,517, of record).

Roof et al. discloses that progesterone has been shown to have neuroprotective effects following traumatic brain injury in rat patients, and/or in injured nervous system including the severity of postinjury cerebral edema in rat patients. See the entire article especially abstract and introduction.). It is also disclosed that postinjury cerebral edema causes substantial cell loss. See page 2. Roof et al. particularly discloses the administration of progesterone to male rat patients after suffering medical frontal cortex contusions, i.e., initial treatment of progesterone with a pharmaceutical carrier, oil, by injection, 4 mg/kg, was given 5 min post-injury and the remaining injections, 4 mg/kg, were given 6 hour post-injury and again once each 24-hours (see the last paragraph of page 3 to page 4 the 3rd paragraph), or the initial treatment after injury occurs at least within 2 hours of contusion (see page 6-7). Roof et al. also teaches that other agents or compounds such as vitamin E and methylprednisolone are known to be useful in the claimed method with progesterone (see page 3, lines 5-9). It is also disclosed that postinjury cerebral edema causes substantial cell loss. See page 2.

Note that Roof et al. discloses that the effective amount of progesterone to be administered is in the range of 4 mg/kg, which is the instant claimed amount in claim 8 herein and also within the claimed effective amounts, about 1 μg/kg- 50 mg/kg, in claim 7 herein.

Roof et al. does not explicitly teach the administration of progesterone metabolite, allopregnanolone for the treatment methods therein.

Backstrom et al. teach that allopregnanolone is a progesterone metabolite, which is useful for treating CNS disorders

Gee et al. discloses that progesterone metabolites including the particular progesterone metabolite, allopregnanolone, are useful in a method for treating seizure disorders in a patient in need thereof (see particularly col.4 lines 37-39; col.1 lines 17-21; Table 2 at col.13-14). Gee et al. also discloses that the beneficial effect of progesterone is related to the conversion of progesterone to the active metabolites including allopregnanolone since the metabolites and derivatives possess higher potency and efficacy than progesterone (see col.17 lines 29-35).

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopregnanolone for treating traumatic central nervous system injury because 1) Roof et al. teach that progesterone is known to have neuroprotective effects in injured nervous system following traumatic brain injury in rat patients, and/or in injured nervous system including the severity of postinjury cerebral edema in rat patients, 2) allopregnanolone is a progesterone metabolite which is well known to be useful for treating CNS disorders according to Backstrom, and 3) Gee et al. teaches that allopregnanolone possess higher potency and efficacy than progesterone.

Thus, one of ordinary skill in the art at the time of invention would have motivated to administer progesterone metabolite, allopregnanolone with reasonable success of

treating traumatic central nervous system injury associated disorders with superior efficacy and potency than progesterone.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roof et al., Roof et al. (*Restoration Neurology and Neuroscience*, 1992, vol.4, 425-427, of record), in view of Backstrom et al. (US 6,455,516, PTO-892), and Gee et al. (Re. 35,517, of record).

Roof et al. discloses that progesterone is useful in treating brain edema resulting from traumatic brain injury or following contusion injury in male and female rat patients. See the entire article especially abstract and introduction. Roof et al. particularly discloses the administration of progesterone with a pharmaceutical carrier, peanut oil, to male rat patents after suffering medical frontal cortex contusions, i.e., initial treatment of progesterone by injection, 4 mg/kg, was given 1 hour after contusion and the remaining injections, 4 mg/kg, were given 6, 24 and 48 hour post-injury (see the 3rd paragraph of page 426), or the initial treatment after injury occurs at least within 2 hours of contusion (see page 6-7).

Note that Roof et al. discloses that the effective amount of progesterone to be administered is in the range of 4 mg/kg, which is the instant claimed amount in claim 8 herein and also within the claimed effective amounts, about 1 μg/kg- 50 mg/kg, in claim 7 herein.

Roof et al. does not explicitly teach the administration of progesterone metabolite, allopregnanolone for the treatment methods therein.

Backstrom et al. teach that allopregnanolone is a progesterone metabolite, which is useful for treating CNS disorders

Gee et al. discloses that progesterone metabolites including the particular progesterone metabolite, allopregnanolone, are useful in a method for treating seizure disorders in a patient in need thereof (see particularly col.4 lines 37-39; col.1 lines 17-21; Table 2 at col.13-14). Gee et al. also discloses that the beneficial effect of progesterone is related to the conversion of progesterone to the active metabolites including allopregnanolone since the metabolites and derivatives possess higher potency and efficacy than progesterone (see col.17 lines 29-35).

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopregnanolone for treating traumatic central nervous system injury because 1) Roof et al. teach that progesterone is known to have neuroprotective effects in injured nervous system following traumatic brain injury in rat patients, and/or in injured nervous system including the severity of postinjury cerebral edema in rat patients, 2) allopregnanolone is a progesterone metabolite which is well known to be

useful for treating CNS disorders according to Backstrom. Furthermore, Gee et al. teaches that allopregnanolone possess higher potency and efficacy than progesterone.

Thus, one of ordinary skill in the art at the time of invention would have motivated to administer progesterone metabolite, allopregnanolone with reasonable success of treating traumatic central nervous system injury associated disorders with superior efficacy and potency than progesterone.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roof et al. in view of Backstrom et al. (US 6,455,516, PTO-892), and Gee et al. (Re. 35,517, of record) as applied to claims 1-12, and 15-20 above, and further in view of Weinshenker et al. (5,068,226).

Roof et al. in view of Backstrom et al. and Gee et al. is as discussed above.

The prior art does not expressly disclose the employment of cyclodextrin as the carrier for the particular progesterone metabolite, allopregnanolone.

Weinshenker et al. discloses that cyclodextrins are broadly known to be useful as carriers for improving the delivery of active agents such as steroids, e.g., cyclodextrins

enhancing the solubility of progesterone 2000 fold and similar effects are observed with other steroids such as prednisolone (see col.6 lines 20-32).

One having ordinary skill in the art at the time the invention was made would have been motivated to employ cyclodextrin as the carrier for the particular progesterone metabolite, allopregnanolone since that cyclodextrins are broadly known to be useful as carriers for improving the delivery of active agents such as steroids, e.g., cyclodextrins enhancing the solubility of progesterone 2000 fold and similar effects are observed with other steroids such as prednisolone according to Weinshenker et al.

Applicant's arguments filed 11/28/2005 with respect to the rejections of record in the previous Office Action have been fully considered but are moot in view of the new ground(s) of rejection above. These remarks are believed to be adequately addressed by the obvious rejection presented above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER